

**REMARKS**

In response to the Examiner's objections, Applicants have amended the specification to correct an obvious typographical error in paragraph [0070]. Applicants have also amended embedded hyperlinks found in paragraphs [0048] and [0057].

Applicants have canceled claim 42 without prejudice.

Applicants make these amendments expressly without waiver of their right to file for and to obtain claims directed to the canceled or amended subject matter in this application or in divisional or continuing applications claiming priority and benefit herefrom.

None of these amendments adds new matter. Their entry is requested. Upon entry of these amendments, claims 24-27, 31, 35-41, 43-53, 80, and 97-98 will be pending. Claims 28-30, 32-34, 62-79, and 81-96 stand withdrawn. Claims 1-23, 42, and 54-61 are canceled.

**The Office Action**

Applicants acknowledge the Examiner's withdrawal of the rejection of claim 31 under 35 U.S.C. 112, second paragraph.

Applicants also acknowledge the Examiner's withdrawal of the rejection of claims 24-27, 31, 39 and 40 under 35 U.S.C. 102(b).

Applicants also acknowledge the Examiner's withdrawal of the rejection of claims 24-27, 31, 35-53, and 80 under 35 U.S.C. 103(a).

**Objections to the Specification**

The Examiner has objected to the disclosure for having a typographical error in paragraph [0070] of the specification. Applicants have obviated this objection by amending the specification to correct this typographical error.

The Examiner has also objected to the disclosure for containing an embedded hyperlink. Applicants have obviated this objection by deleting the embedded hyperlinks in paragraphs [0048] and [0057] and replacing them with textual descriptions of the website addresses.

In view of the foregoing amendments, the Examiner's objections are moot.

Claim Rejection under 35 U.S.C. 112, second paragraph

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Solely to expedite prosecution and to place the application in condition for allowance, Applicants have canceled claim 42. The Examiner's rejection is moot in view of this amendment.

Claim Rejections under 35 U.S.C. 102

Claims 24-27, 31, 35, 39-44, 47-48, 50, 80, and 97 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Dijkstra *et al.* (*Journal of the European Academy of Dermatology and Venereology*, 15:550-554 (2001); hereinafter "Dijkstra"). According to the Examiner, Dijkstra discloses photodynamic therapy with violent [sic] light and topical  $\delta$ -aminolaevulinic acid ( $\delta$ -ALA). Applicants traverse.

Dijkstra cannot anticipate the present claims because it is directed to a technology unrelated to the instant invention. Specifically, Dijkstra describes an application of photodynamic therapy to treat skin lesions. Photodynamic therapy uses a light source not as a means to deliver a bioactive substance across the skin, as is presently claimed, but as an energy source to initiate a photochemical reaction in a photosensitive compound. The photosensitive compound reacts with the light source to produce a product that can act on cells (e.g., is toxic to cells). Therefore, in Dijkstra, light is used to produce therapeutically useful cytotoxic drugs (*i.e.*, singlet oxygen and other free radicals) from an otherwise inactive pro-drug (*i.e.*,  $\delta$ -ALA) (see Dijkstra, page 550, introduction).  $\delta$ -ALA and its products selectively accumulate in hyperproliferative cells after passive transdermal diffusion of the compound through the skin. The continuous light source in Dijkstra is not pulsed, which is different from the "pulsed" incoherent light recited in the claims, and is only used for catalysis of the photochemical reaction of  $\delta$ -ALA after it enters the body. In other words, Dijkstra's light source plays no role in the delivery of  $\delta$ -ALA across the cellular surface or the skin. In fact, the light source in Dijkstra is applied only after 8 hours of application of  $\delta$ -ALA to the skin under plastic occlusion (see Dijkstra, page 551, paragraphs 5-6). This is necessary because premature application of light in

Dijkstra will convert δ-ALA to the therapeutically useful singlet oxygen and other free radicals before δ-ALA even reaches the target cells.

Thus viewed, in Dijkstra, a different type of light source (*i.e.*, continuous vs. pulsed) is used, and the “illuminating” step must be carried out after the “permeating” step, not before. Dijkstra therefore does not meet all the elements of the pending claims, and cannot anticipate the pending claims.

By contrast, the instant invention relates to the use of pulsed incoherent light to increase uptake of a biologically active substance through the skin. The methods of the instant invention are distinct from Dijkstra in at least three ways. First, unlike Dijkstra which is reliant on passive diffusion to deliver δ-ALA, the instant invention uses a light source to actively deliver a substance through the cellular surface on the skin. Second, the light source in the claimed invention does not change the chemical properties of the substance being delivered. By contrast, the light source in Dijkstra is specifically chosen to cause a chemical reaction in the delivered compound and alters the properties of the compound. Third, the light source in the claimed invention is a pulsed light source, while the light source in Dijkstra is continuous, not pulsed.

Because of the completely different nature of the techniques, the methods taught in Dijkstra is not designed, and in fact cannot increase the uptake of a biologically active substance since the continuous light source is applied to the skin after the compound has already permeated through the skin by passive diffusion.

For the foregoing reasons, Dijkstra does not anticipate the claimed invention. Reconsideration and withdrawal of this rejection are respectfully requested.

#### Objections to the Claims

The Examiner has objected to claims 36-38, 45-46, 49, 52-53, and 98 for being dependent upon a rejected base claim. Applicants believe that base claim 24 is allowable, thus making dependent claims 36-38, 45-46, 49, 52-53, and 98 also allowable. Applicants respectfully request that the Examiner withdraw his objection to dependent claims 36-38, 45-46, 49, 52-53, and 98.

The Examiner has also objected to claim 51 for reciting the abbreviation cps at its first occurrence in the claims. Applicants have obviated this objection by amending claim 51 to recite

"cycles per second (cps)." Applicants believe that the objection is moot in view of this amendment.

The Examiner has also objected to claim 97 for comprising non-elected subject matter. Applicants submit that claim 97 is a dependent claim of claim 24. If claim 24 is allowable (as Applicants believe), claim 97 must be rejoined under 37 CFR 1.141 (see page 2, first paragraph of the Office Action). Applicants respectfully request that the Examiner withdraw his objection to claim 97.

### CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000.

Applicants believe no fee is due in connection with the filing of this response. If, however, any fee is due, please charge any deficiency in the fees that may be due (or credit any overpayment if appropriate) to **Deposit Account No. 18-1945**, from which the undersigned is authorized to draw, under **Order No. 002162-0001**.

Dated: April 14, 2008

Respectfully submitted,

By \_\_\_\_\_

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